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Postpartum Thyroiditis – Should Postpartum Mothers Be Routinely Screened for Thyroid Dysfunction Without Prior Indication of a Thyroid Condition?

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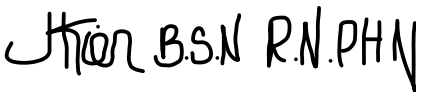
Signature: 

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Abstract

Postpartum thyroiditis (PPT) is a triphasic phenomenon that affects women who clinically are without thyroid disease prior to pregnancy but develop PPT in the first year postpartum or after a spontaneous/induced abortion (Vimalachandran, 2019). Recognition of thyroid dysfunction and possible differentials can augment the providers' ability to appropriately counsel and treat the patient. PPT affects about 5-10% of all women; of those that develop PPT, one in five patients will develop permanent hypothyroidism and require lifelong treatment (Burman, 2019). The etiology, risk factors, clinical course, prognosis, and treatment of PPT will be reviewed as it correlates with the clinical relevance of screening patients for potential thyroid dysfunction.

Postpartum Thyroiditis – Should Postpartum Mothers Be Routinely Screened for Thyroid Dysfunction Without Prior Indication of a Thyroid Condition??

Background

Thyroid disorders are among the most common endocrine conditions evaluated and treated by clinicians during the antenatal and postnatal periods apart from diabetes (Tingi et al., 2016). Postpartum thyroiditis is an autoimmune destruction of the thyroid gland, which is characterized by three (triphasic thyroid pattern) phases; thyrotoxic, hypothyroid, and a euthyroid phase (Pearce, 2015). Physiological changes of the thyroid along with pathological function are most affected during the antenatal period and the year following parturition resulting in a combination of increased metabolic demand, often causing an onset, exacerbation, or relapse of autoimmune diseases (Tingi et al., 2016). Postpartum thyroiditis does not always manifest clinically, indicating the importance of identification of this differential by the clinician (Gibson & Nelson-Piercy, 2018).

During a healthy pregnancy, the thyroid increases in size and vascularity, the thyroid-stimulating hormone reaches the upper limit of normalcy and decreases while the thyroxine (T4) and the triiodothyronine (T3) increases by fifty percent (Grossman & Porth, 2014). The increases in T3 and T4 are needed to maintain free thyroxine (fT4) within normal limits as pregnancy increases thyroxine-binding globulin giving women a high reserve within the thyroid gland (Grossman & Porth, 2014). Pregnancy is described as a "biological stress test" by endocrinologists, and without underlying conditions, the thyroid can compensate "flawlessly" (Stagnaro-Green et al., 2019). However, thyroid dysfunction antenatal and postnatal is associated with adverse outcomes for both the mother or baby, including anemia, miscarriage, fetal growth restriction, gestational diabetes, pre-eclampsia/gestational hypertension, pre-term birth/delivery,

neurodevelopmental delay, stillbirth, respiratory distress and fetal death (Gibson & Nelson-Piercy, 2018; Nguyen & Mestman, 2019; Stagnaro-Green et al., 2019; Yalamanchi & Cooper, 2015)

Pearce (2015) and Vimalachandran (2019) have found that in PPT lymphocytic inflammation of the thyroid initially leads to a transient thyrotoxicosis which can last two to four months up to six to nine weeks; symptoms are typically mild and go unnoticed because the patient is adapting to other physiological changes in the postpartum period with a newborn/baby. If screened during this time, the T4 can have marked elevation in comparison to T3, and as these thyroid stores deplete a progression through a euthyroid to hypothyroid phase before thyroid recovery can occur. One-third of patients will experience the triphasic pattern, and one third can experience a biphasic pattern with either a thyrotoxicosis or hypothyroidism. The reoccurrence of PTT has been documented in nearly 70% of diagnosed patients.

Screening for thyroid dysfunction is not routine antenatal, nor postnatal, and is typically only completed by targeted screening secondary to the patients' risk factors. The goal of this review is to determine if standardizing routine screening can prevent postpartum mothers from developing permanent hypothyroidism if screened, diagnosed, and treated within an appropriate timeframe. Clinical indication for an appropriate postpartum thyroiditis versus hypothyroidism differential diagnosis is essential due to their potential for different clinical courses and treatments.

Case Report

Elizabeth was a 37-year-old patient that presented to the clinic for evaluation of ongoing fatigue, dry skin, weight gain of 15lbs., and difficulty with memory and concentration. The patient stated she noticed symptom onset three months prior initially with her weight gain, and fatigue. The patient did not have any recent changes in her typical day, attended a local gym but resorted to the sauna due to decreased endurance, and unusual exhaustion. During assessment, Elizabeth revealed an ongoing inability to stay on task for long periods. She denied any change in sleep or intake patterns but had been having difficulty passing bowels; denied any OTC intervention but had increased her water, fruits, and vegetable intake. The patient did have a primary care provider, which she presented to only when needed, which she contacted before presenting and had pre-ordered fasting labs completed.

The patient was a G3P3 that was currently breastfeeding - her youngest child was born nine months ago without complication – her menses are irregular, she contributes this to breastfeeding, natural family planning with unknown last menstrual cycle. Besides the recent onset of stated symptoms patient had unremarkable health history, all health maintenance and immunizations were up to date, no known food, seasonal or drug allergies, and she was only taking two over the counter medications; a women's multivitamin, and a generic probiotic.

Her physical examination revealed a well-developed and nourished woman, vitals, 130/80 blood pressure, 76 pulse, 16 respiration, 100% on room air, 97.8 tympanic temperature, 71 inches in height, and 81 kilograms in weight. No evidence of thyroid enlargement, tenderness, nodules or lymphadenopathy, cardiac assessment revealed regular rate and rhythm, no jugular venous distention, and clear lung sounds bilaterally, normoactive bowel sounds in all four

quadrants, soft, non-tender, with no masses. The patient did have generalized xerosis cutis; her affect mildly flat with some forgetfulness, memory, and judgment were appropriate for age.

Elizabeth's diagnostic exam revealed an unremarkable complete blood count (CBC), comprehensive metabolic panel (CMP), glycated hemoglobin test (HgA1C) of 5.4%, vitamin D of 40ng/mL, negative urinalysis, human chorionic gonadotropin (hCG), C-reactive protein (CRP) of 4.0mg/L and a marked elevation of her thyroid-stimulating hormone (TSH) of 7.0mU/L and a decrease in thyroxine (T4) at 0.25mcg/dL.

Based on Elizabeth's presentation of symptoms, her history, physical exam, and diagnostic findings, hypothyroidism was suspected. Per Naidu et al. (2019), it is not uncommon for patients to present with complaints of chronic fatigue, slowed thinking, constipation, dry skin, menstrual disturbances, and a modest weight gain with primary hypothyroidism. Physical exam usually reveals dry, coarse, or thickened skin, hair loss, or brittle hair, coarsening of voice, goiter, periorbital puffiness, swelling of hands, and feet, bradycardia, reduced systolic blood pressure, or increased diastolic blood pressure and delayed deep tendon reflexes. Diagnostic test results for hypothyroidism include an elevated TSH, a decreased serum free T4.

However, because Elizabeth was nine months postpartum, she also had clinical suspicion for the triphasic thyroid hormone pattern of postpartum thyroiditis (PPT). Clinical presentation of PPT can vary, and because the patient did not have any risk factors before indicating the need for thyroid function screening antenatal nor postnatal, a thyroid peroxidase (TPO) antibody titer was added on to her previously collected labs. With the treatment guidelines/indications being similar for primary hypothyroidism and symptomatic postpartum thyroiditis the patient was treated with 25mcg of daily Levothyroxine and directed to return for follow-up in four to six weeks for a recheck on her TSH and T4 and potential increase of her medication until a

therapeutic index is reached or she can discontinue medication therapy (Naidu et al., 2019; Vimalachandran, 2019). Levothyroxine excretion, while breastfeeding reviewed with the patient and not contraindicated (Hale & Rowe, 2019).

Literature Review

Research was conducted through the University of North Dakota's School of Medicine & Health Sciences Library, with primary search through Clinical Key, PubMed, and CINAHL. Postpartum thyroiditis and hypothyroidism were used with identified MeSH subheadings, complications, diagnosis, drug therapy, epidemiology, immunology, mortality, prevention and control, pharmacokinetics, pharmacology, statistics, and numerical data, and trends. Descriptors included English, female adults (age 19-44), publication within the past five years in the form of – Systematic Reviews, Meta-analysis, Practice Guidelines, Case Reports, Literature, and Narrative Reviews. Limitations yielded near 300 results; factors requiring removal included non-topic correlation, no abstract, no full-text availability, professional reply excerpts, duplication, and exceptional circumstance and consideration of interlibrary loan unavailability. Fifteen articles were identified with relevancy for this review.

In order to avoid adverse maternal and fetal outcomes, early diagnosis and management of thyroid disruption, both antenatal and postnatal is vital. Due to the wide range of physiological changes that are experienced during pregnancy with the thyroid gland and hormones, diagnosis can often be challenging for the clinician. Clinical symptom presentation for postpartum thyroiditis can vary depending on the course of phase in dysfunction; symptoms of the hyperthyroid phase are often described as mild with generalized complaints of fatigue, palpitations, irritability, sleep disturbance, increased sweating, and heat intolerance (Kellerman, 2020; Nguyen & Mestman, 2019; Vimalachandran, 2019). Within the hypothyroid phase patients

typically can present with complaints of constipation, irregular menstrual bleeding, impaired memory, or concentrations, fatigue, generalized aches, and pains, weakness, dry skin, hair loss, cold intolerance, difficulty with weight loss, or mild weight gain (Kellerman, 2020; Nguyen & Mestman, 2019; Vimalachandran, 2019). The etiology with thyroid dysfunction and postpartum depression remains unclear; however, patients with postpartum depression are recommended to be screened for a thyroid disorder (Iwen & Lehnert, 2018). Postpartum thyroiditis can impact milk letdown and the mother's ability to breastfeed successfully; women that demonstrate poor lactation should also be evaluated for thyroid disorders (Nguyen & Mestman, 2019).

The physical exam of PPT is similar to those that occur in nonpregnant patients and is dependent on the phase in which the woman is presenting; examination of the thyroid may reveal a diffusely enlarged painless gland with a pebbly like texture, a painless small nontender firm goiter, or the thyroid gland can be normal without any palpable masses (Kellerman, 2020; Vimalachandran, 2019). Signs of hyperthyroidism may reveal hyperreflexia, tachycardia, with or without atrial fibrillation; a hypothyroid presentation may include delayed reflexes, nonpitting edema, dry skin, coarse/thickened skin, reduced systolic blood pressure, increased diastolic blood pressure, and bradycardia, or the patient could have a benign exam and present without any signs or symptoms suggestive of a thyroid disorder (Kellerman, 2020; Naidu et al., 2019; Vimalachandran, 2019). Distinguishing differences in hyper/hypothyroidism from healthy physiological changes in pregnancy and the postpartum period can be difficult; however, features suggestive of thyroid disorders that preceded pregnancy indicate a need for screening (Gibson & Nelson-Piercy, 2018).

Due to the complexity of trimester-specific reference ranges for testing of thyroid function, this report only reflects postpartum screening and an antibody predictor of PPT within

the first trimester with normal reference ranges. Interpretation of diagnostic laboratory testing for hypothyroidism usually includes an elevated TSH and decreased serum free T4, with an anti-TPO antibody positivity marker being the best predictor of PPT (Vimalachandran, 2019). However, the screening of asymptomatic antenatal and postnatal women for thyroid disruption remains controversial and not routinely recommended allowing variation in diagnosing and management practices.

Guidelines & Recommendations

Current guideline trends gathered within the literature presume a targeted screening approach rather than a universal approach that identifies women that are at high risk for developing thyroid dysfunction during pregnancy or in the postnatal period. Targeted screening is guided on three principles per Stagnaro-Green et al., (2019), risk factors identify patients that are predisposed to the disease of interest, screening individuals with those risk factors can help identify a majority of patients with a lower cost derived with targeted screening versus the downside of false positives and negatives. Kellerman (2019) and Mcdermott (2019) also found that the debate on universal screening varies from society to society with substantial opinion consideration from endocrinologists, obstetricians, gynecologists, and governmental agencies; however, targeted screening for predisposed patients all trend in similarity.

The American College of Obstetricians and Gynecologists (ACOG) recommendations require testing of high-risk women that are symptomatic or have a personal history of any autoimmune diseases (Yalamanchi & Cooper, 2015). The Endocrine Society supports a "case-finding" approach in conjunction with generalized guidelines across clinical resources such as up-to-date and 5minute consult which includes: patients that live in areas of moderate to severe iodine insufficiency, symptomatic, familial, or personal history of thyroid disease, or have any of

the following: thyroid peroxidase (TPO) antibodies, goiter, >30 years of age, diabetes, head, or neck irradiation, recurrent miscarriages, preterm deliveries, two, or more pregnancies, obesity, infertility, prior thyroid surgery (Burman, 2019; Donnay Candil, 2015; Naidu, 2019; Ross, 2020; Smith et al., 2017 Vimalachandran, 2010; Yalamanchi & Cooper, 2015). The American Thyroid Association (ATA) recommendations are similar of the Endocrine Society and clinical references with the addition that patients who have received recent administration of iodinated radiologic contrast agents or are currently prescribed amiodarone or lithium receive screening for thyroid dysfunction in the first trimester (Yalamanchi & Cooper, 2015).

Studies have shown that a targeted screening and case finding approach may fail to identify near 30-80% of thyroid dysfunction in the antenatal and postnatal periods (Pearce, 2015; Smith et al., 2017). Nevertheless, a unanimous consensus remains about testing asymptomatic non-at-risk patients, with interest, however, regarding their availability, reliability, and potential for cost-effectiveness versus not testing patients. The recommendation for screening of thyroid dysfunction in high-risk patients should be completed in the first trimester with a thyroid peroxidase antibody (TPO-Ab) titer. The TBO can detect inflammation of the thyroid gland and can also predict dysfunction, autoimmune disorder(s), and other non-organ-specific antibodies, which can precipitate adverse pregnancy complications (Borba et al., 2019; Pearce, 2015). Per Vimalachandran (2019), TBO-Ab+ is the most predictive marker for PPT; women known to have the presence of antibodies within the first trimester should have their thyroid-stimulating hormone (TSH) measured at six to twelve weeks' gestation and repeated at six months postpartum or as clinically indicated. Women with positive antibodies usually have hypothyroidism between three to eight months postpartum, with 80% of them spontaneously

resolving at one year postpartum. However, of those that do not resolve 30-50% of them can develop permanent hypothyroidism within ten years.

Detection

Though there are not universal screening guidelines for asymptomatic antenatal and postnatal women, LeFevre (2015) discusses the theory of the pros and cons of detection and why they need to be considered. The benefits of early detection, like many conditions, may be beneficial for long term morbidity and mortality from permanent hypothyroidism, cancers, and/or cardiovascular diseases. The U.S Preventive Services Task Force (USPSTF) has found inadequacies in screening asymptomatic women for thyroid dysfunction in correlation to beneficial cardiovascular disease outcomes; however, they concluded early detection and treatment does not have clinically meaningful improvements in blood pressure, body mass index (BMI), bone density, lipid levels, or cognitive function. Harms of early detection included false-positive results, psychological effects of patient labeling/diagnosing, over-diagnosing, overtreating, and being wrongly treated by inexperienced clinicians added Stagnaro-Green et al., (2019). Harmful impact of late detection can cause a multitude of complications including persistent hypothyroidism, congenital disabilities, goiter, cardiac issues, infertility, and myxedema (Burman, 2020).

Special considerations

Factors that can influence a patients' TSH results include timing, prescribed medications, over-the-counter supplements, and their current state of health. In times of illness, during pregnancy, and in the postpartum period or when a patient may have other comorbidities such as protein malnutrition, hepatic failure, or nephrotic syndrome evaluation of thyroxine T4 and triiodothyronine T3 would be indicated (Naidu et al., 2019; Nguyen & Mestman, 2019). The

thyroid-stimulating hormone is in a state of constant fluctuation, proving that it is not the best lone indicator of overall thyroid function in the postpartum period; once a patient reaches the hypothyroid state during PPT, there is a marked decrease in the T4 and T3 (Burman, 2019; Naidu, 2019; Paulson, 2019; Ross, 2020; Vimalachandran, 2010; Yalamanchi & Cooper, 2015). Nguyen and Mestman (2019) also stated that when a TPO-Ab+ is positive, the thyroglobulin antibody (TG-Ab) may also be positive; however, it is not a typical diagnostic marker of PPT. Lastly, in the postpartum period, thyroid hormone autoantibodies (TH-Ab) can interfere with appropriate evaluation of thyroid function due to their elevated concentrations and binding properties but resolve by 48 weeks postpartum. No reports have concluded their prediction of PPT.

Nyugen and Mestman (2019) concluded that studies evaluating the prevention of PPT have been unsuccessful and have not been able to prove a reduction of risk in developing permanent hypothyroidism if diagnosed and treated early augmenting nonuniversal routine screening guidelines. Hypothyroidism has been reported in 2-21% of patients one year postpartum with reports up to 54%. Thirty to fifty percent of women that had PPT reported a diagnosis of permanent hypothyroidism as early as three years post-delivery, up to 12 years.

Evaluation

Due to the complexity of evaluating thyroid function in the postpartum period and non-universal screening guidelines, Paulson (2019) describes a common discussion across the literature to not treat pharmacologically based on one set of diagnostic results if the patient is asymptomatic because of the transient prediction of returning to euthyroid state and the sensitivity and specificity of TSH levels. Recommendation to repeat a TSH, or fT4 is based on slight deviation out of reference range which should be completed at the same laboratory; please

note diagnosing hypothyroidism and evaluating TSH levels to assess replacement therapy are not included in this literature and do not reflect the prior statements (Paulson, 2019). However, the USPSTF states that TSH is the gold standard for detecting thyroid dysfunction and that it should be performed at three to six-month intervals to rule out or confirm abnormal findings (LeFevre, 2015). Optimal screening intervals and frequencies are unknown.

Another statement that should be taken into consideration by Tandeter and Fraenkel (2018) indicates that once a patient is pharmaceutical, they are always pharmaceutical; with clinical guidelines to start therapies, there are not always clear cut guidelines to discontinue therapy once a therapeutic index is reached. The literature shines a light on the recent publication of medications that should or could be stopped, such as antihypertensives and statins. However, in patients with any variation of hypothyroidism, these patients usually receive lifelong therapies despite the restoration of thyroid function. Variances within the literature describe select few patients that are treated with levothyroxine and have been able to titrate off the medication once a euthyroid level is reached – variations of patients include deficiency in vitamin d, iodine uptake and other autoimmune disorders respectfully (Burman, 2019; Naidu, 2019; Paulson, 2019; Ross, 2020; Vimalachandran, 2010; Yalamanchi & Cooper, 2015).

Treatment

Approaching the patient with PPT is primarily based on the clinicians' index of suspicion for hypothyroidism and correlation with clinical symptoms, physical examination, and laboratory values. Levothyroxine is the principle monotherapy treatment for hypothyroidism but is dependent on different factors. Asymptomatic patients with mild thyroid function test abnormalities do not require pharmacological therapy; however, they should have their TSH and free T4 monitored for evaluation of resolution, or to detect permanent hypothyroidism (Burman,

2019). Symptomatic hypothyroidism or a TSH above 10mU/L requires T4 replacement; dependent on the degree of elevation determines the appropriate dose of Levothyroxine (Burman, 2019).

The prediction of permanent hypothyroidism is inefficacious; therefore, patients are titrated off at 12 months postpartum for a reevaluation of spontaneous resolution of their thyroid function, those that do not have spontaneous resolution of thyroid function require therapy and annual evaluations' of TSH as indicated (Burman, 2019; Gibson & Nelson-Piercy, 2018; Pearce, 2015; Vimalachandran, 2019). Patients that desire future pregnancies should receive education and the recommendation to continue T4 supplementation along with breastfeeding women (Nguyen & Mestman, 2019).

Conclusion

Throughout the literature, the question remains, should we be screening non-at-risk postpartum mothers for thyroid dysfunction? There seems to be insufficient data supporting the recommendation for routine screening in asymptomatic patients that are not predisposed to thyroid disorders. In the absence of strong evidence indicating a need for universal routine screening, the decision to screen, treat, and manage this condition lies primarily on an appropriate history and physical by the clinician. Mandated screening does not exist; however, recommended screening of thyroid function does occur when patients reach certain ages' dependent on the guidelines a clinician chooses to follow (Naidu et al., 2019). The literature on screening asymptomatic patients for thyroid dysfunction was partially scarce, though the clinical question prompts an appropriate differential diagnosis consideration when treating women of childbearing age.

Learning Points

- Understanding the physiological changes and pathological function of the thyroid and its dysfunction that a patient may encompass during pregnancy is vital for the best maternal and fetal outcomes.
- Though there is conflicting research on the indication for routine screening of postpartum mothers, the clinician must be able to identify this differential within the practice setting when working with antenatal and postnatal women.
- If a clinician chooses to routinely screen patients within their practice setting, the patient should be informed and fully aware of the potential clinical benefits and harms of screening within the antenatal and postnatal periods.
- If the clinician chooses to screen asymptomatic postnatal women, be confident in the clinical decision to treat or not treat. (If you screen, know why you are screening, and what you are going to do about it).
- Currently, no known interventions exist to prevent hypothyroidism (Kellerman, 2019).

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